ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 799

[OPTS-42033; BH-FRL 2341-2]

Cresols; Proposed Test Rule

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

SUMMARY: Under section 4 of the Toxic Substances Control Act (TSCA), EPA is proposing that manufacturers and processors of cresols test these chemicals for carcinogenicity, mutagenicity, teratogenicity, reproductive effects, neurotoxicity, skin sensitization and subchronic toxicity. The testing being proposed will be performed according to protocols adopted by the Agency. EPA is not proposing to require any additional environmental effects testing at this time. However, EPA is also soliciting public comments on the decision not to propose environmental effects testing for cresols. This notice constitutes EPA's response to the Interagency Testing Committee's (ITC) designation of cresols as priority candidates for testing.

DATES: Submit written comments on or before September 9, 1983. If persons request an opportunity for oral comment by August 25, 1983, EPA will hold a public meeting on September 26, 1983, on this rule in Washington, D.C. For further information on arranging to speak at the meeting see unit VI of this preamble.

ADDRESS: Submit written comments in triplicate to: TSCA Public Information Office (TS-793), Office of Pesticide and Toxic Substances, Environmental Protection Agency, Rm. E-108, 401 M St. SW., Washington, D.C. 20460.

Include the document control number [OPTS-42032] on all submissions.

FOR FURTHER INFORMATION CONTACT: Jack P. McCarthy, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Rm. E-545, 401 M St. SW., Washington, D.C. 20460, Toll Free: (800-424-9065), In Washington, D.C.: (554-1404), Outside the USA: (Operator-202-554-1404).

SUPPLEMENTARY INFORMATION:

I. Introduction

Section 4(e) of TSCA (Pub. L. 94-469, 90 Stat. 2003 *et seq.*; 15 U.S.C. 2601 *et seq.*) established an Interagency Testing Committee (ITC) to recommend to EPA a list of chemicals to be considered for testing under section 4(a) of the Act. The ITC may designate substances on the list for priority consideration for requiring testing by EPA.

The ITC designated cresols for priority consideration in its Initial Report, published in the **Federal Register** on October 12, 1977 (42 FR 55026). The ITC recommended that industry test cresols for the following health effects: carcinogenicity, mutagenicity, teratogenicity and other chronic effects. The ITC also recommended testing for environmental effects, specifically chronic effects in fish and other aquatic organisms.

The ITC's recommendations were based on the large volume of cresols produced in the United States. It was estimated in the ITC's report that the U.S. production of cresols in 1975 was about 90 million pounds. The ITC also reported an annual release rate of approximately 45 million pounds. In addition, the ITC was concerned that the manufacture and use of cresol-containing products could result in substantial occupational exposure and high general population exposure.

Under section 4(a)(1) of TSCA, EPA must require testing of a chemical substance to develop health or environmental data if the Agency finds that:

> (A) (i) the manufacture, distribution in commerce, processing, use, or disposal of a chemical substance or mixture, or that any combination of such activities, may present an unreasonable risk of injury to health or the environment,
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> (ii) there are insufficient data and experience upon which the effects of such manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture or of any combination of such activities on health or the environment can reasonably be determined or predicted, and
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> (iii) testing of such substance or mixture with respect to such effects is necessary to develop such data; or
>
> (B) (i) a chemical substance or mixture is or will be produced in substantial quantities, and (I) it enters or may reasonably be anticipated to enter the environment in substantial quantities or (II) there is or may be significant or substantial human exposure to such substance or mixture,
>
> (ii) there are insufficient data and experience upon which the effects of the manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture or of any combination of such activities on health or the environment can reasonably be determined or predicted, and
>
> (iii) testing of such substance or mixture with respect to such effects is necessary to develop such data.

EPA uses a weight of evidence approach in making a section 4(a)(1)(A)(i) finding in which both exposure and toxicity information are considered to make the finding that the chemical may present an unreasonable risk. For the section 4(a)(1)(B)(i) finding, EPA considers only production, exposure and release information to determine if there is substantial exposure or release. For the findings under both section 4(a)(1)(A)(ii) and 4(a)(1)(B)(ii), EPA examines toxicity and fate studies to determine if existing information is adequate to determine or reasonably predict the effects of human exposure to or environmental release of the chemical. In making the third finding that testing is necessary, EPA considers whether any ongoing testing will satisfy the information needs for the chemical and whether testing which the Agency might require would be capable of developing the necessary information.

EPA's process for determining when these findings can be made is described in detail in EPA's first and second proposed test rules as published in the **Federal Register** of July 18, 1980 (45 FR 48528) and June 5, 1981 (46 FR 30300). The section 4(a)(1)(A) finding is discussed in 45 FR 48528, and the section 4(a)(1)(B) finding is discussed in 46 FR 30300.

In evaluating the ITC's testing recommendations concerning cresols, EPA considered all available relevant information including the following: Information presented in the ITC's report recommending testing consideration; production volume, use, exposure, and release information reported by manufacturers of cresols under the TSCA section 8(a) Preliminary Assessment Information Rule (40 CFR Part 712); health and safety studies submitted by the manufacturers of cresols under the TSCA section 8(d) Health and Safety Data Reporting Rule (40 CFR Part 716); and published and unpublished data available to the Agency. Based on its evaluation, as

described in this preamble and the accompanying technical support document, EPA is proposing health effects testing requirements for cresols under section 4(a)(1)(A) and 4(a)(1)(B). EPA tentatively has determined that additional environmental effects testing should not be required. However, due to the absence of chronic toxicity data for fish and invertebrates in freshwater and saltwater systems, EPA is soliciting comments on the need for additional environmental effects testing. By these actions, EPA is responding to the ITC's designation of cresols for testing consideration.

II. Cresols

A. Profile

Cresols (C_7H_8O) is a chemical category consisting of three cresol isomers; *ortho*-cresol (*o*-cresol), *meta*-cresol (*m*-cresol), and *para*-cresol (*p*-cresol). Cresols are commercially available as individual isomers or as mixtures. Approximately, 172–200 million pounds of cresols are either produced in or imported into the United States each year. The EPA Toxic Substances Inventory records that approximately 72 million pounds of *o*-cresol; 32 million pounds of *m*-cresol and 62 million pounds of *p*-cresol were produced in the United States in 1977.

Cresols are used as wire enamel solvents and as organic intermediates in the manufacture of phenolic resins and phosphate esters. Additional uses of either individual isomers or mixtures are in the production of several herbicides, as cleaning compounds and disinfectants, and in ore flotation.

B. Findings

The EPA is basing its proposed testing on the authority of section 4(a)(1)(B) of TSCA. Additionally, for mutagenicity and oncogenicity, the Agency is basing this proposal on the authority of section 4(a)(1)(A).

EPA finds that each of the three cresol isomers is manufactured, processed, and used in substantial quantities, which may result in substantial human exposure. Furthermore, EPA finds that there are insufficient data available to either reasonably determine or predict the result of this exposure in the areas of carcinogenic, mutagenic, teratogenic, reproductive, neurotoxic, skin sensitivity, and subchronic health effects. These findings are based on the following information:

1. There are substantial amounts of cresols produced in or imported into the United States each year. The annual U.S. production volume of cresols is estimated to be approximately 169 million pounds, with another 17 million pounds imported into the United States each year. Each of the three cresol isomers is individually produced in substantial quantities. Of the total 169 million pounds produced domestically, 43 percent is *o*-cresol, 37 percent is *p*-cresol and 20 percent is *m*-cresol.

2. Estimates indicate that between 600,000 and 1.2 million people are exposed to cresols each year via manufacturing, processing and/or use activities.

3. EPA finds that there are insufficient data on all of these cited human health effects from which to reasonably determined or predict the result of exposure to cresols, and that testing of cresols for these effects is necessary to develop such data.

4. EPA does not believe that the rule will result in a loss to society of the benefits of cresols because the Agency's economic evaluation has shown that the economic impact of testing these substances will be minimal.

In addition, EPA has found that (a) there is evidence of potential unreasonable human health risks from mutagenic and carcinogenic effects resulting from the manufacture, processing and use activities associated with cresols, and that while there are existing data which support this belief with respect to these effects, (b) these existing data are inadequate to reasonably predict or determine the effects of these exposures to cresols, and (c) testing is necessary for these effects. Therefore, EPA believes that requiring testing of cresols for mutagenicity and carcinogenicity can also be based upon section 4(a)(1)(A) of TSCA.

The analyses on which the above findings are based, are presented in the Cresols Support Document which is available from the TSCA Assistance Office (TAO). The ITC recommendations and EPA's proposed testing requirements are summarized in the following tables:

Effect	ITC recommendation	EPA proposed testing [1]
Skin sensitization	–	×
Chronic effects	×	× [2]
Mutagenicity	×	×
Carcinogenicity	×	× [3]
Teratogenicity	×	×
Reproductive effects	–	×
Neurotoxicity	×	×
Environmental effects	×	– [3]

[1] Subchronic proposed in lieu of full chronic.
[2] Test substance(s) to be selected based on mutagenicity testing.
[3] EPA will determine if testing is needed based upon public comments.

In addition, the Agency has concluded that the following human health effects are adequately characterized and, therefore, that no further testing should be required at this time: Acute toxicity (lethality); acute skin and eye irritation, and skin corrosivity. The Agency has also concluded that available information is sufficient to evaluate the chemical fate and bioconcentration potential of cresols, and therefore no further testing in these areas is being proposed at this time.

With respect to environmental concerns, the Agency finds that the release of cresols to the environment is high. About 3.5 million pounds per year are released to the atmosphere, while the estimated annual release of cresols as solid wastes is 4.2 million pounds. The aqueous compartment may receive as much as 11.2 million pounds per year from dispersed use of cleaning compounds. It is estimated that about 80 percent of that volume is discharged to sewage treatment plants and will be biodegraded resulting in an expected annual release of as much as 2.8 million pounds of cresols to natural waters.

While there is no existing chronic aquatic effects data for cresols, the Agency believes that information exists which allows EPA to reasonably predict that exposure of aquatic organisms to cresols should not cause chronic effects. Therefore, the Agency has made a preliminary judgment that no additional environmental effects testing is needed at this time. This judgment is based on monitoring information which indicates that the ambient concentrations of cresols found in aquatic systems are expected to be minimal and will not be acutely toxic to aquatic organisms based on existing data for acute effects. In addition, analyses have been conducted for cresols using EPA's Exposure Analsysis Modeling Systems (EXAMS) and the Environmental Partitioning Model (ENPART). The results of EXAMS and ENPART, using actual discharge and flow rates from a cresols manufacturing plant, indicate that the expected concentrations of cresols, after treatment, will be 0.0016 mg/L—one mile from point of discharge, 0.0014 mg/L—five miles from point of discharge, and finally 0.00094 mg/L—30 miles from point of discharge. These numbers reflect the concentration levels that would be expected in the winter months, when microbial degradation rates would be the lowest, and with maximum effluent discharge rates.

Therefore, while the ITC recommended testing for environmental effects, the Agency may be able to reasonably predict that levels of cresols may not cause chronic effects. However, this preliminary decision not to propose

environmental effects testing for cresols one for which further input by erested parties will be particularly lpful to the Agency. Therefore, EPA is soliciting public comment on the need for chronic toxicity data generation.

The public comments received in response to this Federal Register notice will be instrumental in assisting the Agency in evaluating its decision not to propose environmental effects testing for cresols. If, after the public comments are reviewed and evaluated, and the Agency is convinced that its preliminary decision is inappropriate for cresols, then the Agency will require, in the final rule for cresols, that environmental effects testing be performed.

In that event, the environmental effects testing shall be performed for the purpose of developing data on the chronic toxicity of cresols to aquatic organisms in saltwater and freshwater systems. The following environmental effects studies would be included as required testing in the final rule: Freshwater vertebrate early life stage testing in rainbow trout, freshwater invertebrate chronic test in *Daphnia* sp., saltwater vertebrate early life stage in *Menidia* sp., and saltwater invertebrate chronic in Mysid shrimp.

The Agency has determined that sufficient information does exist for acute toxicity and that no additional acute testing is needed. In addition, the Agency has determined that while there is substantial release of cresols to the soil, this route of environmental exposure is not expected to be a problem. Cresols are readily biodegraded by soil microflora and are mobile in soils. Therefore, cresols will not persist in soils and will probably be leached, due to their water solubility, into the aquatic environment where they will be acted upon by degrading microorganisms. The Agency has also determined that cresols released to the atmosphere are not expected to create an exposure problem. Cresols are not expected to persist in the atmosphere because (1) cresols have low estimated half-lives of less than 1 day, (2) they are sensitive to photolysis, and (3) the water solubility of cresols may be expected to cause transport of cresols from the atmosphere to the soil or aqueous environment.

C. Test Substance

EPA is proposing for the subchronic toxicity, mutagenicity, carcinogenicity, teratogenicity, reproductive effects, eurotoxicity, and skin sensitization esting that *o*-cresol, *m*-cresol and/or *p*-cresol of at least 98 percent purity shall be used as the test substance(s).

Each individual isomer will be tested in the subchronic toxicity, teratogenicity, reproductive effects, neurotoxicity, and skin sensitization studies. However, some of the cresol isomers have previously been tested in individual mutagenicity tests included in the proposed battery. Therefore, in some instances, not all of the isomers will be tested in each mutagenicity test. The test substance(s) in the oncogenicity bioassays will be determined from the results obtained in the proposed mutagenicity test battery as further explained in section 7.4 of the Cresols Support Document.

Each isomer has exhibited different chemical and toxicological properties in previous testing. EPA has determined that because of these differences, one of the cresol isomers could not satisfactorily be tested in all the proposed testing as a representative of all three.

Furthermore, it is not generally acceptable for an equimolar mixture of the three cresol isomers to be the test substance in the prescribed health effects testing. The Agency is primarily interested in the health effects attributable to individual cresol isomers.

With regard to mutagenic and carcinogenic effects, a mutagenicity testing battery has been proposed for cresols, with testing endpoints that could result in oncogenicity bioassays for individual cresol isomers. This proposed tiered mutagenicity testing scheme has been designed specifically for cresols. It has been conceived to serve both as an indicator of mutagenic potential, an ITC concern, and also as a procedure to identify the test substance(s) to be used in any subsequent oncogenicity testing. While the ITC recommended carcinogenicity testing for cresols, EPA finds that the proposed mutagenicity testing scheme is an appropriate and scientifically valid first testing tier in screening for oncogenicity.

Several testing endpoints in this mutagenicity battery could result in oncogenicity bioassays for individual cresol isomers. However, if, after the completion of the entire mutagenicity test battery, each of the three cresol isomers produce only negative results, thereby not triggering any 2-year bioassays, then a mixture of the three isomers shall be tested in a full 2-year oncogenicity bioassay. If the mutagenicity tests on individual isomers are negative, the rule will require that a mixture be tested. EPA requests comments on the appropriate composition for such a mixture. The decision to propose an oncogenicity bioassay for isomeric mixture is based on the fact that, in previous mutagenicity testing, an equimixture of the three cresol isomers has had positive results. However, as the Agency is primarily interested in the health effects of the individual isomers, the isomers will be initially screened as the potential bioassay test substances, prior to any testing of an isomeric mixture.

D. Persons Required to Test

Section 4(b)(3)(B) specifies that the activities for which the Administrator makes section 4(a) findings (manufacture, processing, distribution, use and/or disposal) determines who bears the responsibility for testing. Manufacturers are required to test if the findings are based on manufacturing, ("manufacture" is defined in section 3(7) of TSCA to include "import"). Processors are required to test if the findings are based on processing. Both manufacturers and processors are required to test if the exposures giving rise to the potential risk occur during use, distribution, or disposal. Because EPA has found that the manufacturing, processing, and use of cresols give rise to exposures that may lead to an unreasonable risk, EPA is proposing that persons who manufacture or process, or who intend to manufacture or process these chemicals at any time from the effective date of this test rule to the end of the reimbursement period be subject to the rule. The end of the reimbursement period, ordinarily will be 5 years after the last final report is submitted. As discussed in Unit II.F, EPA expects that manufacturers will conduct testing and that processors will ordinarily be exempted from testing.

Because TSCA contains provisions to avoid duplicative testing, not every person subject to this rule must individually conduct testing. Section 4(b)(3)(A) of TSCA provides that EPA permit two or more manufacturers or processors who are subject to a test rule to designate one such person or a qualified third person to conduct these tests and submit data on their behalf. Section 4(c) provides that any person required to test may apply to EPA for an exemption from that requirement.

E. Development and Adoption of Study Plans

EPA proposed generic test methodology requirements (generic test standards) for various health effects in the Federal Register of May 9, 1979 (44 FR 27334) and July 26, 1979 (44 FR 44054). In response to concerns about rigid generic test methodology requirements, EPA changed its approach

for providing test standards for TSCA section 4 test rules and issued generic test methodology guidelines to replace previously proposed generic test methodology requirements. (See the Federal Register of March 26, 1982; 47 FR 13012.) The Health Effects Guidelines have been published by the National Technical Information Service (NTIS) under publication number PB 82-232984. Good Laboratory Practice (GLP) standards will continue to be promulgated as generic requirements.

Under the new approach, test rule development will be a two-phase process. In Phase I, test rules will be promulgated for individual chemicals, specifying the health or environmental effects characteristics for which test data are to be developed and the reporting requirements. In Phase II, following promulgation of a test rule, those persons subject to the rule will be required to develop study plans for the development of data pertaining to the effects and characteristics specified in the rule. For guidance in preparing study plans, it is recommended that the TSCA Health Effects Test Guidelines, published by NTIS (PS 82-232984), be consulted. Additional guidance may be obtained from the Organization for Economic Cooperation and Development (OECD) Test Guidelines and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS under publication number PB 83-153916.

Sponsors must submit their study plans to EPA within 90 days from the effective date of the test rule. After an opportunity for public comment, EPA will issue a final rule adopting the study plans as proposed or modified. The approved and adopted study plans will become the enforceable test requirements and will serve as the chemical specific test standards for the test rule. Testing will also be subject to EPA's generic GLP standards. Modification to the adopted study plans can be made only with EPA approval.

EPA intends to issue a procedural rule which will set out the details of the two-phase rulemaking process. That procedural rule will apply to the test rule for cresols and all other test rules. Information on this proposed procedure appears in the July 18, 1980 Federal Register (45 FR 48512), which describes the proposed exemption policy and procedures, in March 26, 1982 Federal Register (47 FR 10312) which provides the policy statement on the test rules development process and in the proposed test rule for diethylenetriamine, see the April 29, 1982 Federal Register (47 FR 18390). The final procedural rule will be issued before the cresols rule is promulgated. If there are significant changes in the final procedural rule, EPA may allow a short period of supplementary comment on the cresols proposal.

For the purposes of announcing the carcinogenicity test if it is needed, the Agency will publish an announcement in the Federal Register announcing the receipt of the mutagenicity data, the results of the testing and the need for the carcinogenicity testing, and the particular test substance. This Notice will then start the portion of the rule requiring carcinogenicity testing. Persons subject to the rule will follow the existing mechanisms for submission of study plans within the allowed time.

EPA has been reevaluating this two-phase rulemaking process with a view to improving its efficiency. The Agency is considering a modification as follows. EPA would conduct its rulemaking in a single phase. The proposed test rule would contain all the necessary elements: The basis for the testing decision, who must test, the tests to be performed, and the test standards which would apply to the specific tests. After receiving comments on all aspects of the rule, EPA would promulgate the final rule. Once the final rule was in effect, manufacturers and processors subject to the rule would be required to announce their intention to test or apply for exemption.

The key difference between this modified approach and current two-phase approach is that the protocols which would become the test standards for the required tests would be proposed by EPA in phase I rather than being submitted by test sponsors in phase II. EPA believes such a change would be appropriate in light of its experience in rulemaking under section 4 and would be likely to speed the process for adopting test rules. To implement this approach EPA is considering proposing that testers be able to choose to perform the required tests under any of the appropriate protocols in the FIFRA guidelines, OECD guidelines, and TSCA guidelines. During the comment period, interested persons would be able to comment on the details of these protocols and could, if desired, propose alternative protocols.

If EPA decides to take this modified approach, the Agency will publish later this year supplementary proposls for cresols and other recent proposed test rules setting out protocols which would be the test standards, and seeking comment on those protocols. EPA believes these supplementary proposals would result in final test rules faster than under the current two-phase process.

EPA solicits comments on this proposed modification of the test rules process.

F. Exemption Procedures

Within 30 days after the effective date of the final rule, each cresol manufacturer or group of cresol manufacturers must either (1) notify EPA that it intends to conduct or sponsor testing and to submit study plans for the required tests, or (2) apply for an exemption on a belief that testing will be performed by others. Study plans must be submitted 90 days after the effective date of this rule. If no manufacturer notifies EPA of its intent to sponsor testing, EPA will inform manufacturers that their exemptions will not be granted and will give them an opportunity to submit study plans in compliance with this rule.

Processors of cresols will not be required to apply for an exemption, submit study plans or conduct testing unless manufacturers do not submit study plans and conduct testing. EPA will issue a notice in the Federal Register requiring processors to submit notices of intent to test or apply for an exemption, submit study plans and conduct testing. No exemptions will be granted until a study plan for each of the required tests is received and approved.

EPA has determined that the three cresol isomers are not equivalent because each isomer has exhibited different chemical and toxicological properties in previous testing. In applying for an exemption, manufacturers must state which isomer or isomers they manufacture. If the substance manufactured contains more than one cresol isomer, then the percent isomer composition or range of percent isomer composition should be given.

EPA proposed exemption procedures for section 4 test rules in the Federal Register of July 18, 1980 (45 FR 48512). EPA intends to issue these procedures as a final rule shortly. If there are significant changes in the exemption procedures, EPA may allow a short period of supplementary comment on the cresols proposals.

G. Reporting Requirements

EPA is proposing that all data be reported in accordance with the EPA GLP Standards to appear in 40 CFR Part 792. EPA has reviewed public comment on the proposed GLP Standards and is now developing final GLP standards.

The final GLP Standards will apply to this rule.

EPA is required by TSCA section 4(b)(1)(C) to specify the time period during which persons subject to a test rule must submit test data. These deadlines will be established in the Phase II rulemaking in which study plans are approved, or in a subsequent FR notice if EPA changes its policy as described in section E, above.

TSCA section 14(b) governs Agency disclosure of all test data submitted pursuant to section of TSCA. Upon receipt of data required by this rule, the Agency will publish a notice of receipt in the **Federal Register** as required by section 4(d).

H. Enforcement Provisions

Section 15(1) of TSCA makes it unlawful for any person to fail or refuse to comply with any rule or order issued under section 4. Section 15(3) of TSCA makes it unlawful for any person to fail or refuse to (1) establish or maintain records, (2) submit reports, notices, or other information, or (3) permit access to or copying of records required by the Act or any regulation issued under TSCA. The Agency considers that failure to comply with any aspect of a section 4 rule may be judged to be a violation of sections 15(1) and 15(3) of TSCA.

Additionally, TSCA section 15(4) makes it unlawful for any person to fail or refuse to permit entry or inspection as required by section 11. Section 11 applies to any "establishment, facility, or other premises in which chemical substances or mixtures are manufactured, processed, stored, or held before or after their distribution in commerce * * *". The Agency considers a testing facility to be a place where the chemical is held or stored and, therefore, subject to inspection. Laboratory audits/inspections will be conducted periodically in accordance with the procedures outlined in TSCA section 11 by only designated representatives of the EPA for the purpose of determining compliance with any final rule for cresols. These inspections may be conducted for purposes which verification that testing as begun, that schedules are being met, that reports accurately reflect the underlying raw data and interpretations and evaluations thereof, and that the studies are being conducted according to TSCA standards and the test standards established in the Phase II rule.

Violators of TSCA may be subject to criminal and civil liability. Persons who submit materially misleading or false information in connection with the requirement of any provision of this rule may be subject to penalties calculated as if they never submitted their data. Under the penalty provision of section 16 of TSCA, any person who violates section 15 could be subject to a civil penalty of up to $25,000 per day for each violation. Each day of operation in violation may constitute a separate violation. (This would also be applicable to manufacturers or processors who fail to submit a letter of intent to perform testing or an exemption request and who continue manufacturing or processing after the deadlines for such submissions. Knowing or willful violations could lead to the imposition of criminal penalties of up to $25,000 for each day of violation and imprisonment for up to one year. Other remedies are available to EPA under sections 7 and 17 of TSCA, such as seeking an injunction to restrain violations of TSCA section 4 and the seizure of chemical substances manufacture or processed in violation of the rule.

Individuals, as well as corporations, could be subject to enforcement actions. Section 15 and 16 of TSCA apply to "any person" who violates various provisions of TSCA. EPA may, at its discretion, proceed against individuals as well as companies themselves. In particular, this includes individuals who report false information or who cause it to be reported. In addition, the submission of false, fictitious, or fraudulent statements is a violation under 18 U.S.C. 1001.

I. Issues for Public Comment

1. The Agency has proposed a mutagenicity testing scheme with testing endpoints that could result in oncogenicity bioassays for individual cresol isomers. The Agency is requesting comments on the tiered testing approach for cresols, in light of the fact that the ITC recommended carcinogenicity testing for cresols. Does the mutagenicity scheme, as designed, serve the purpose of screening the three isomers for potential oncogenicity? Does a negative result for an isomer in the mutagenicity screen reasonably eliminate the need to require a full bioassay for that isomer?

2. In previous mutagenicity assays, an equimixture of the three cresol isomers was tested. The results of the equimixture in the unscheduled DNA synthesis assay, the mouse lymphoma assay, the sister chromatid exchange assay and the cell transformation, with activation, assay were positive. In the event that the cresol isomers, when tested individually, produce negative results in all of the assays in the full mutagenicity testing scheme, no oncogenicity bioassays would be triggered for any of the cresol isomers. The present testing scheme is designed so that positive results in any of the six mutagenicity assays, for any individual isomers would trigger a 2-year oncogenicity bioassay for that isomer. However, the cresol mixture did produce positive results in some of these same tests. The Agency is proposing to require that an isomeric mixture of cresols be tested in a 2-year oncogenicity bioassay if all the individual isomers produce negative results in the mutagenicity testing scheme.

However, cresols are commercially processed into a wide variety of mixtures, composed of two or three isomers in any number of proportional combinations with each other and with other chemicals. Therefore, the Agency is requesting comments on the suitable test substance in a two-year oncogenicity bioassay. What would be a representational isomeric mixture which could serve as a test substance, in the event that none of the individual cresol isomers trigger a two-year bioassay in the mutagenicity testing screen?

3. The ITC recommended that cresols be tested for chronic effects in fish and other aquatic organisms. The Agency believes that there is substantial release and exposure to the environment by cresols, and has tentatively concluded that there is sufficient information which, when evaluated, allows the Agency to reasonably predict that cresols do not pose either an acute or a chronic aquatic toxicity hazard. This information upon which the evaluation was based, includes ambient concentrations predicted through computer models, available acute toxicity data, monitoring data, and known bioconcentration, biodegradation and persistence values.

The Agency in this proposed rule has an acute toxicity to ambient concentration ratio of over 10,000 at a point approximately 30 miles downstream of the discharge. Further, the Agency believes that given this ratio there is a low likelihood of chronic effects. However, the Agency acknowledges that it does not have an absolute assurance that chronic toxicity could not occur. If comment convinces EPA that it cannot reasonably predict that cresols will not be chronically toxic at known or projected concentration levels, it would require freshwater and saltwater chronic tests on aquatic vertebrates (rainbow trout and *Menidia* sp.) and a chronic toxicity study on aquatic invertebrates (*Daphnia* sp. and Mysid shrimp). The Agency recognizes that data, particularly those obtained

from predictive modeling, are open to many different interpretations. Therefore, the Agency is soliciting comments on the amount and type of data which the Agency should have before making a decision that this data allows it to reasonably predict that effects will not occur.

III. Economic Analysis of Proposed Rule

To assess the potential economic impact of this proposed rule, EPA has prepared a Level I economic evaluation that examines the costs of the required testing and analyzes four market characteristics of the chemical: (1) Demand sensitivity, (2) cost characteristics, (3) industry structure, and (4) market expectations.

The Level I analysis of cresols, which estimates a total testing cost of from $800,000 for the minimum set of tests to $5 million for the maximum set of tests, indicates that the potential for adverse economic effects due to the estimated testing costs is low. This conclusion is based on the following observations:

1. Stable or moderate growth is expected in most markets for cresols.

2. The production of coproducts to cresols would mitigate the potential for impact of incremental test costs.

3. The relative magnitude of the test cost is minor, i.e., on an annualized unit cost basis, the upper end of the cost range is equivalent to $0.012 per pound for *o*-cresol and for the mixed cresols (*m*-cresol and *p*-cresol) the cost is $0.009 per pound. This represents 2.1 percent of price for *o*-cresol, 0.6 percent for cresylic acid, and 1.0 percent for all other cresols.

4. Demand in most of the markets does not appear very sensitive to small increases in price.

Because the Level I analysis indicates very little potential for an adverse economic impact, EPA has determined that a more comprehensive and detailed Level II economic evaluation is not needed for cresols.

IV. Availability of Test Facilities and Personnel

Section 4(b)(1) requires EPA to consider "the reasonably foreseeable availability of the facilities and personnel needed to perform the testing required under the rule." Therefore, EPA conducted a study to assess the availability of test facilities and personnel to handle the additional demand for testing services created by section 4 test rules and test programs negotiated with industry in place of rulemaking. Copies of the study, "Chemical Testing Industry: Profile of Toxicological Testing, October, 1981," can be obtained from NTIS, under publication number PB 82-140773.

On the basis of this study, the Agency believes that there will be available resources to perform the testing in this proposed rule.

V. Environmental Impact Statement

EPA is not required to prepare Environmental Impact Statements (EIS), under the National Environmental Policy Act (NEPA), 41 U.S.C. 4321, for test rules. EPA has determined that voluntary preparation of an EIS is not appropriate for regulations issued under section 4 of TSCA. For further discussion of EPA's EIS policies, see the preamble to the Agency's rules for compliance with NEPA published in the Federal Register of November 6, 1979 (44 FR 64174).

VI. Public Meetings

If persons wish to present comments on this proposed rule to EPA officials who are directly responsible for developing the rule and supporting analyses, EPA will hold a public meeting on September 26, 1983, in Washington, D.C. This meeting is scheduled after the deadline for submission of written comments, so that issues raised in the written comments can be discussed by EPA and the public commenters. Information on the exact time and place of the meeting is available from the TSCA Assistance Office (TAO), Toll Free: (800-424-9065). In Washington, D.C.: (554-1404). Outside the U.S.A. (Operator-202-554-1404).

Persons who wish to attend or present comments at the meeting should call the TAO by August 25, 1983. While the meeting will be open to the public, active participation will be limited to those persons who arranged to present comments and to designated EPA participants. Attendees should call the TAO before making travel plans because the meeting will not be held if members of the public do not wish to make oral comments.

The Agency will transcribe the meeting and include the written transcript in the public record. Participants are invited, but not required, to submit copies of their statements prior to or on the day of the meeting. All such written materials will become part of EPA's record for this rulemaking.

VII. Public Record

EPA has established a public record for this rulemaking docket number [OPTS-42033] which is available for inspection in the OPTS Reading Room from 8:00 a.m. to 4:00 p.m., Monday through Friday, except legal holidays in Rm. E-107, 401 M St. SW., Washington, D.C. This record includes the basic information the Agency considered in developing this proposal, and appropriate Federal Register notices. The Agency will supplement the record with additional information as it is received. This record includes the following information:

(1) Federal Register notices pertaining to this rule consisting of:

(a) Notice of proposed rule on cresols.

(b) Notice containing the ITC designation of cresols to the Priority List (42 FR 55026, October 12, 1977).

(c) Notices relating to EPA's health effects test guidelines and EPA Good Laboratory Practice Standards.

(d) Notice of proposed rule on exemption policy and procedures.

(e) Notice of proposed rulemaking on reimbursement policy and procedures.

(2) Support Documents: consisting of:

(a) Cresols support document.

(b) Economic analysis support document.

(c) Human exposure assessment support document.

(3) Communications before proposal consisting of:

(a) Written public and intra-agency memoranda and comments.

(b) Summaries of telephone conversations.

(c) Meeting summaries.

(d) Reports—published and unpublished factual materials, including contractors' reports.

VIII. Classification of Rule

Under Executive Order 12291, EPA must judge whether a regulation is "Major" and, therefore, subject to the requirement of a Regulatory Impact Analysis. The regulation for these chemical substances is not major because it does not meet any of the criteria set forth in section 1(b) of the Order. First, the actual annual cost of the testing prescribed for cresols is less than $1.3 million over the testing and reimbursement period. Second, because the cost of the required testing will be distributed over a large production volume, the rule will have only very minor effects (less than 2.1 percent a year) on producers' costs or users' prices for this chemical. Finally, taking into account the nature of the market for this substance, the low level of costs involved, and the expected nature of the mechanisms for sharing the costs of the required testing, EPA concludes that there will be no significant adverse economic impact of any type as a result of this rule.

This proposed regulation was submitted to the Office of Management

and Budget (OMB) for review as required by Executive Order 12291. Any comments from OMB to EPA, and any EPA response to those comments, are included in the public record.

IX. Regulatory Flexibility Act

Under the Regulatory Flexibility Act, (15 U.S.C. 601, *et seq.*, Pub. L. 96-354, September 19, 1980), EPA is certifying that this test rule, if promulgated, will not have a significant impact on a substantial number of small businesses for the following reasons:

1. Small processors will not perform testing themselves, or will not participate in the organization of the testing effort.

2. Small processors will experience only minor costs in securing exemption from testing requirements.

3. Small processors are unlikely to be affected by reimbursement requirements.

X. Paperwork Reduction Act

The Paperwork Reduction Act of 1980 (44 U.S.C. 3501 *et seq.*) authorizes the Director of OMB to review certain information collection requests by Federal agencies. The test rule proposed in this notice, if promulgated, could result in the submission of several types information related to the required ting, including study plans and final eports for each test required by persons sponsoring the tests. For the reasons set forth in the **Federal Register** of June 5, 1981 (46 FR 30315), EPA believes that the test rule contained in this notice does not constitute an information collection request as defined in the Paperwork Reduction Act.

(Sec. 4, TSCA (Pub. L. 94-469, 90 Stat. 2003; 15 U.S.C. 2601))

List of Subjects in 40 CFR Part 799

Testing, Environmental protection, Hazardous material, Chemicals.

Dated: June 30, 1983.

William D. Ruckelshaus,
Administrator.

PART 799—IDENTIFICATION OF SPECIFIC CHEMICAL SUBSTANCES TESTING REQUIREMENTS

Therefore, it is proposed that a new § 799.1250 be added to the proposed Part 799 to read as follows:

Subpart A—[Reserved]

Subpart B—Specific Chemical Testing

99.1250 ortho-Cresol (o-cresol), meta-sol (m-cresol) and para-cresol (p-cresol).

(a) *Identification of test substance.* (1) *o*-Cresol (CAS No. 95-48-7), *m*-cresol (CAS No. 108-39-4), and *p*-cresol (CAS No. 106-44-5), each shall be tested in accordance with this part.

(2) *o*-Cresol, *m*-cresol and *p*-cresol of at least 99 percent purity shall be used as the test substances in all tests.

(b) *Persons required to test.* (1) All persons who manufacture or intend to manufacture any cresol isomer or any mixture of cresol isomers from the effective date of this rule to the end of the reimbursement period shall submit study plans, as specified by 40 CFR Part 770, and conduct tests and submit data as specified by this part.

(2) Any person subject to the requirements of this section may apply to EPA for an exemption from study plan submission, testing and data submission. No later than 30 days after the effective date of this rule, each manufacturer of cresols must notify EPA by letter of an intent either to submit a proposed study plan or to be exempted from testing for each test or study required in this rule.

(3) If manufacturers submit study plans, conduct testing, and submit data in a satisfactory manner, processors will be given an automatic exemption by EPA. If manufacturers fail to submit study plans, all persons who process or intend to process cresols from the effective date of this rule to the end of the reimbursement period shall be directed in a special **Federal Register** notice to submit study plans and to conduct tests and submit data as specified by this Part or be in violation of this rule.

(c) *Study plans*—(1) *Testing.* Testing shall be performed using a study plan submitted and approved in accordance with 40 CFR Part 770. All data must be developed and reported in accordance with the EPA Good Laboratory Practice (GLP) standards in accordance with 40 CFR Part 792. Laboratories conducting testing under this rule must adhere to the EPA GLP standards published by the Agency.

(2) *Submission.* (i) Manufacturers of cresols who indicate they will perform testing must submit proposed study plans on or before 90 days after the effective date of this rule. Only one set of study plans should be prepared and submitted by persons who are jointly sponsoring testing.

(ii) If, by the date specified in paragraph (b)(2) of this section, no letter of intent to submit a proposed study plan is submitted by a manufacturer for a test or study required by this rule, EPA will so notify the manufacturers of cresols. If no manufacturer promptly decides to submit a study plan and conduct testing, EPA will publish a **Federal Register** notice of this fact and then (A) no later than 30 days after publication of such a notice, each processor must notify EPA by letter of its intent either to submit a proposed study plan for each test or study that will not be covered by manufacturers' study plans or to be exempted from testing and (B) processors who indicate they will perform testing must submit proposed study plans on or before 90 days after publication of such a notice.

(iii) Manufacturers which do not notify EPA of their intent, either to submit a proposed study plan or to be exempted from testing for each test or study required in this rule, will be considered in violation of the rule beginning on the 31st day after the effective date of the rule. Manufacturers who indicate they will perform testing and which do not submit proposed study plans on or before 90 days after the effective date of this rule will be considered in violation of the rule beginning on the 91st day after the effective date of this rule. Each processor who fails to submit a letter of intent to submit a study plan or to request an exemption when required will also be considered in violation of this rule beginning on the 31st day after publication of the notice described in paragraph (c)(2)(ii) of this section.

(iv) If no study plan is proposed for each test or study required in this rule, every manufacturer and every processor of such chemicals will be in violation of this rule beginning on the 91st day after the publication of the notice described in paragraph (c)(2)(ii) of this section until such a study plan is submitted by an appropriate sponsor.

(3) *Content.* (i) All study plans are required to contain the following information: (A) Identity of the test rule and the specific test requirements of that rule to be covered by the study plan.

(B)(*1*) The names and addresses of the test sponsors.

(*2*) The names and addresses of the responsible administrative officials and project manager(s) in the principal sponsor's organization.

(*3*) The name, address and telephone number of the appropriate individual(s) for oral and written communications with EPA.

(*4*)(*i*) The name and address of the testing facility(ies) including responsible administrative officials and project manager(s) responsible for this testing.

(*ii*) Brief summaries of the training and experience of each professional involved in the study including study director, veterinarian(s), toxicologist(s), pathologist(s) and laboratory assistants.

(C) Identity and data on the substances being tested including

appropriate physical constants, spectral data, chemical analysis and stability under test and storage conditions.

(D) Study protocols, including rationale for: species-strain selection; dose selection (and supporting data); route(s) or method(s) of exposure; a description of diet to be used and its source, including nutrients and contaminants and their concentrations; for *in vitro* test systems, a description of culture medium and its source; and a summary of expected spontaneous chronic disease (including tumors), genealogy, and life span.

(E) Schedule for initiation and completion of major phases of long term tests; schedule for submission of interim progress and final reports to EPA.

(ii) Information given under paragraph (c)(3)(i)(B)(*4*) of this section is not required in proposed study plans if the information is not available at the time of submission; however, the information must be submitted before the initiation of testing.

(4) *Adoption.* Upon receipt of proposed study plans, EPA will publish in the Federal Register a notice requesting comments on the ability of the study plans to ensure that data from the tests are reliable and adequate. EPA will provide a 45-day comment period, and will provide an opportunity for an oral presentation on the request of any person. EPA may extend the comment period if it appears from the nature of the issues raised by EPA's review or public comment that further comment is warranted. Following the close of the comment period, EPA will publish a final rule adopting the study plans as proposed or modified which will become the test standards by which the study will be conducted.

(5) *Modification of study plans during conduct of study*—(i) *Application.* Any test sponsor who wishes to modify the adopted study plan for any test required under this rule must submit an application in accordance with this section. Application for modification shall be made in writing or by phone to the Chief Test Rules Development Branch, with written confirmation to follow within 10 working days. Applications must explain why the modification is necessary.

(ii) *Adoption.* To the extend feasible, EPA will seek comment on all significant substantive changes in study plans. EPA will issue a notice in the Federal Register requesting comments on requested modifications in accordance with section 4(b)(5) of TSCA. However, EPA will act on the requested modification without seeking public comment (A) if EPA believes that an immediate modification to a study plan is necessary in order to preserve the accuracy of an on-going study or (B) if EPA determines that a modification clearly does not pose any significant substantive issues. EPA will notify the sponsor of the Agency's approval or disapproval. When the Agency approves a modification, it will publish a notice in the Federal Register indicating that the study plan has been modified.

(d) *Health effects testing*—(1) *Subchronic inhalation toxicity*—(i) *Required testing.* Ninety-day subchronic inhalation toxicity testing shall be conducted with *o*-, *m*-, and *p*-cresol, individually.

(ii) *Study plans.* For guidance in preparing study plans, it is recommended that the Toxic Substances Control Act (TSCA) Health Effects Test Guidelines for Subchronic Exposure Inhalation Toxicity, published by the National Technical Information Service (NITS) under publication number PB–82–232984, be consulted. Additional guidance may be obtained from the organization for Economic Cooperation and Development (OECD) Test Guidelines for Health Effects and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS under publication number PB 83–153916.

(2) *Mutagenic effects—Chromosomal aberrations*—(i) *Required testing.*—(A) *In vitro* cytogenetics tests shall be conducted with *o*-, *m*- and *p*-cresol, individually.

(B) An *in vivo* cytogenetics test shall be conducted for each isomer which produces a negative result in the *in vitro* cytogenetics test.

(C) A dominant lethal assay shall be conducted for each isomer which produces a positive result in either the *in vitro* or the *in vivo* cytogenetics test.

(D) A heritable translocation assay shall be conducted with each isomer which produces a positive result in the dominant lethal assay.

(E) Further testing for chromosomal aberrations is not required for any isomer which produces a negative result in the *in vivo* cytogenetics test or the dominant lethal assay.

(ii) *Study plans.* For guidance in preparing study plans, it is recommended that the TSCA Health Effects Test Guidelines for Chromosomal Effects, published by NTIS (PB 82–232984), be consulted. Additional guidance may be obtained from the OECD Test Guidelines for Genetic Toxicology, and the FIFRA Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 82–153916).

(3) *Mutagenic effects—Gene Mutation*—(i) *Required testing.* (A) a DNA damage assay shall be conducted with *m*- cresol only.

(B) Sister chromatid exchange (SCE) assays shall be conducted with *m*- and *p*-cresol, individually.

(C) Gene mutation in cells in culture assays shall be conducted with *m*- and *p*-cresol, individually.

(D) A second gene mutation in cells in culture assay, using a different cell line from that used in the first assay, shall be conducted for each isomer which produces a negative result in the first gene mutation in cells in culture assay, specified by paragraph (d)(3)(D) of this section, coupled with positive results in both the DNA damage and SCE assays.

(E) *o*- and *p*-Cresol shall be tested in a *Drosophila* sex-linked recessive lethal (SLRL) test. A *Drosophila* SLRL test also shall be conducted for *m*-cresol if it produces a positive result in the DNA damage assay, SCE assay or either gene mutation in cells in culture assay.

(F) A mouse specific locus assay shall be conducted with each isomer which produces a positive result in the *Drosophila* SLRL.

(G) Further testing for gene mutations is not required for any isomer which produces a negative result in the *Drosophila* SLRL.

(H) Further testing for gene mutations is not required for any isomer which produces a negative result in the second gene mutation in cells in culture assay.

(ii) *Study plans.* For guidance in preparing study plans, it is recommended that the TSCA Health Effects Test Guidelines for Gene Mutations and DNA Effects, published by NTIS (PB 82–232984), be consulted. Additional guidance may be obtained from the OECD Test Guidelines for Genetic Toxicology and the FIFRA Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 83–153916).

(4) *Mutagenic Effects—Cellular Transformation*—(i) *Required testing.* (A) Balb/c 3T3 cellular transformation tests performed without metabolic activation shall be conducted with *m*- and *p*-cresol, individually.

(B)(*1*) *o*-Cresol shall be tested in the cellular transformation test with activation. A Balb/c 3T3 cellular transformation test with metabolic activation shall be conducted with each isomer which produces a negative result

in the cellular transformation test without activation.

(2) If the method of metabolic activation in the cell transformation assay with activation, for the individual cresol isomers, is by feeder layers using rat hepatocytes, then an equimixture of the three isomers shall also be tested under these conditions.

(C) A confirmatory tumor formation *in vivo* assay shall be performed with each isomer which produces a positive result in the cellular transformation test without activation or with activation.

(D) Further testing for cell transformations is not necessary for any isomer which produces a negative result in the cellular transformation test with activation or in the confirmatory tumor formation *in vivo* assay.

(ii) *Study plans.* For guidance in preparing study plans, it is recommended that the following paper be consulted: Heidelberger, et al. 1983. Cell Transformation by Chemical Agents; A Review and Analysis of the Literature; A Report of the USEPA's Gene-Tox Program. *Mutation Research*, Vol. 114, pp. 283–385.

(5) *Carcinogenicity*—(i) *Required testing.* A two-year oncogenicity bioassay shall be conducted with each isomer which produces a positive result in any one of the following tests: *in vitro* cytogenetics test, *in vivo* cytogenetics test, first gene mutation in cells in culture assay, second gene mutation in cells in culture assay, *Drosophila* SLRL and cell transformation confirmatory tumor formation *in vivo* tests. A two-year oncogenicity bioassay shall be conducted with a mixture of *o*-, *m*-, and *p*-cresol, if after the completion of the entire mutagenicity test battery, each of the three isomers produce only negative results, thereby not triggering any 2-year bioassays for individual isomers.

(ii) *Study plans.* For guidance in preparing study plans, it is recommended that the TSCA Health Effects Guidelines for Chronic Exposure—Oncogenicity, published by NTIS (PB 82–232984), be consulted. Additional guidance may be obtained from the OECD Test Guidelines for Health Effects, and the FIFRA Pesticide Registration Guidelines: Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 83–153916).

(6) *Teratogenicity*—(i) *Required testing.* Teratogenicity studies shall be conducted with *o*-, *m*-, and *p*-cresol, individually.

(ii) *Study plans.* For guidance in preparing study plans, it is recommended that the TSCA Health Effects Test Guidelines for Specific Organ/Tissue Toxicity-Teratogenicity, published by NTIS (PB 82-232984), be consulted. Additional guidance may be obtained from the OECD Test Guidelines for Health Effects, and the FIFRA Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 83–153916).

(7) *Reproductive effects*—(i) *Required testing.* Two-generation reproductive effects studies shall be conducted with *o*-, *m*-, and *p*-cresol, individually. Inhalation shall be the route of administration of the test substances in these studies.

(ii) *Study plans.* For guidance in preparing study plans, it is recommended that the TSCA Health Effects Test Guidelines for Specific Organ/Tissue Toxicity—Reproduction/Fertility Effects, published by NTIS (PB 82–232984), be consulted. Additional guidance may be obtained from the FIFRA Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 83–153916).

(8) *Neurotoxicity*—(i) *Required testing.* The following neurotoxicity test battery shall be performed following subchronic inhalation exposure.

(A) A neuropathology test shall be conducted with *o*-, *m*-, and *p*-cresol, individually.

(B) A motor activity test shall be conducted with *o*-, *m*-, and *p*-cresol, individually.

(C) A functional observation battery shall be conducted with *o*-, *m*-, and *p*-cresol, individually.

(ii) *Study plans.* For guidance in preparing study plans, it is recommended that the TSCA Health Effects Test Guidelines for Neurotoxicity, published by NTIS (PB 82–232984), be consulted. Additional guidance may be obtained from the FIFRA Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 83–153916).

(9) *Skin sensitization*—(i) *Required testing.* Skin sensitization studies shall be conducted with *o*-, *m*-, and *p*-cresol, individually.

(ii) *Study plans.* For guidance in preparing study plans, it is recommended that the TSCA Health Effects Test Guidelines for Dermal Sensitization, published by NTIS (PB 82–232984), be consulted. Additional guidance may be obtained from the OECD Test Guidelines for Health Effects, and the FIFRA Pesticide Registration Guidelines; Proposed Data Requirements for Hazard Evaluation: Human and Domestic Animals, published by NTIS (PB 83–153916).

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